VITAMIN D DEFICIENCY- A POSSIBLE CONTRIBUTING FACTOR IN THE AETIOPATHOGENESIS OF ORAL LICHEN PLANUS

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ABSTRACT

BACKGROUND

Lichen planus is a chronic autoimmune disease involving skin and mucous membrane. It is believed to represent an abnormal immune response in which epithelial cells are recognised as foreign, secondary to changes in the antigenicity of the cell surface. Certain epidemiological studies are indicative of significant association between vitamin D deficiency and increased incidence of autoimmune diseases. The aim of the present study is to investigate the role of vitamin D in Oral Lichen planus patients and the relationship between serum vitamin D Levels and different clinical forms of Oral lichen planus.

MATERIALS AND METHODS

A convenience sample of 20 cases who were previously diagnosed as Oral lichen planus patients as per Modified World Health Organisation diagnostic criteria of OLP and OLL (2003), and enrolled in the Department of Oral Medicine & Radiology, were selected. A group of 20 age and sex matched healthy controls were included. 25-Hydroxyvitamin D [25(OH) D] Levels were measured by ECLIA (Electrochemiluminescence immunoassay) method in patients and control group.

RESULTS

Statistically Significant Association (P-value<0.05) of serum vitamin D levels was seen in patients with Oral lichen planus.

CONCLUSION

The results of our study suggest that Vitamin D levels may have an important role in the aetiopathogenesis of the disease or may be one of the contributory factors that determines the progression and prognosis of the disease, and as such it is needed that a study with a larger sample size may be conducted in order to establish the role of vitamin D in the aetiopathogenesis of Oral Lichen planus.

KEYWORDS

Oral Lichen Planus, 25-Hydroxyvitamin D, Erosive Lichen Planus.

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BACKGROUND

Lichen planus is a chronic autoimmune disease involving skin and mucous membranes. It can affect the oral mucosa, genital mucosa, skin, scalp and nails.[1]

The term Lichen planus was the first described by Erasmus Wilson in 1869. The aetiology of the condition is still not very clear as it appears to be complex and multifactorial. It affects only 0.52% of the population. Although it is widely recognised in adults, its occurrence is very low in children. A number of aetiological factors may be responsible like genetic, immunological, systemic diseases, graft versus host disease, infective agents, medication, hypersensitive dental materials, and stress.[2,3]

It commonly affects the middle-aged patients[2] and has a female predilection. Oral lichen planus (OLP) is also seen in children, although it is rare.[4,5]As it is evident from the literature that the aetiology of Oral lichen planus is complex and multifactorial, an attempt has been made in the present study to find out any possible correlation between the serum levels of Vitamin D and different types of Oral Lichen planus.

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Aetiology

The precise aetiology of lichen planus is still not very clear. However, Lichen planus is believed to result from an abnormal T-cell-mediated immune response in which basal epithelial cells are recognised as foreign because of changes in the antigenicity of their cell surface.[6] Current data suggest that oral lichen planus is a T-cell-mediated autoimmune disease in which autocytotoxic CD8+ T cells trigger the apoptosis of oral epithelial cells.[7] The CD8+ cytotoxic T cells may trigger keratinocyte apoptosis through activation of the cells by an antigen associated with major histocompatibility (MCH) class I on basal keratinocytes.[7]

Certain diseases and agents, such as viral and bacterial infections, autoimmune diseases, medications, vaccinations and dental restorative materials have been found to be associated with Oral lichen planus. In a study conducted by Moravvej et al[8] in 2007, it was found that statistically significant differences in H. pylori infection between patients with lichen planus and a control group was present. However, an aetiologic role for H. pylori in lichen planus is not yet properly established. A strong association between hepatitis C viral infection and OLP has been demonstrated by Carrozzo et al.[9] However, the association of OLP with HCV infection

appears to be dependent on geographical heterogeneity. Various studies have investigated the association of candida infection and oral lichen planus but failed to establish as an aetiological factor.

Van Belle et al[10] has reviewed role of vitamin D in autoimmune diseases like Type 1 diabetes, systemic lupus erythematosus, inflammatory bowel disease, rheumatoid arthritis, asthma, multiple sclerosis, and in infectious diseases. Moreover various epidemiological evidences indicate a significant association between vitamin D deficiency and an increased incidence of autoimmune diseases. As is evident from the literature that vitamin D has immunomodulatory effects and as such may have a vital role in the pathogenesis of T-cell-mediated autoimmune diseases.

MATERIALS AND METHODS

In the present case-control study, a convenience sample of 20 cases that were previously diagnosed as Oral lichen planus patients and were enrolled in the Department of Oral Medicine & Radiology, were selected. A group of 20 healthy controls who were matched on the criteria of age and sex were enrolled in the study. Controls were selected from the patients who were visiting the Department of Oral Medicine & Radiology for routine dental checkup and did not have any red or white oral lesions present.

Inclusion Criteria

Patients who were selected in the present study had been diagnosed with Oral lichen planus as per Modified World Health Organisation Diagnostic Criteria of OLP and OLL (2003). Consent was obtained from the patients after which a detailed medical history was recorded followed by a thorough clinical examination.

Patients were selected in the age group of 20 -70 years from either gender.

Exclusion Criteria

Patients who had received Vitamin D as a part of management of any medical condition/disease were excluded from the study (e.g.- rickets, osteoporosis, osteomalacia, fractures, etc.).

Blood samples of the OLP group and Control group were obtained. Vitamin D status was determined by ECLIA (Electrochemiluminescence immunoassay) method for both the groups. According to the serum 25(OH)D levels, each given participant was graded as Normal, Insufficient & Deficient with the normal range being 30-70ng/mL,21-29 ng/mL as insufficient and ≤20 ng/mL was considered as deficient.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were summarised in the form of means and standard deviations and categorical variables were summarised as percentages. Chi-square test was employed to determine association of Oral lichen planus with vitamin D levels. Graphically the data was presented by bar diagrams. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

RESULTS

Statistically Significant Association (P-value<0.05) of serum vitamin D levels was seen in patients with Oral lichen planus.(Table -1) The association of age with respect to different forms of Oral Lichen Planus was observed and it was seen that the mean age of patients with Erosive lichen planus was 37.2 years with standard deviation of ±12.69 years, Reticular lichen planus was 41.7 years with standard deviation of ±11.19 years and Reticular lichen planus with erosive component was 47.8 years with standard deviation of ±7.79 years. The P- value obtained was 0.326, (Table-2). Association of Oral lichen planus with respect to gender was seen. Chi -square test was performed and was found as: Chi-square=0.952; the P–value obtained was 0.621. (Table-3).

A comparison based on vitamin D levels among the cases and controls was made. Chi -square test was performed and was found as: Chi-square=4.80; the P–value obtained was 0.0285 which was found to be a statistically significant difference (P-value<0.05). (Table-4).

Oral Lichen Planus	Vitamin D Level			
	Normal		Decreased	
	No.	% Age	No.	% Age
Erosive lichen planus	1	8.3	4	50.0
Reticular lichen planus	9	75.0	1	12.5
Reticular with erosive component	2	16.7	3	37.5
Total	**12**	**100**	**8**	**100**
Chi-square=7.917; P-value=0.019*				

Table 1. Showing Association of Oral Lichen Planus with Vitamin D Levels

*Statistically Significant Association (P-value<0.05)

Oral Lichen Planus	Age (Years)		P-value
	Mean	SD	
Erosive lichen planus	37.2	12.69	0.326
Reticular lichen planus	41.7	11.19	
Reticular with erosive component	47.8	7.79	

Table 2. Showing Association of Oral Lichen Planus with Age

Oral Lichen Planus	Male		Female	
	No.	% Age	No.	% Age
Erosive lichen planus	2	33.3	3	21.4
Reticular lichen planus	2	33.3	8	57.1
Reticular with erosive component	2	33.3	3	21.4
Total	**6**	**100**	**14**	**100**
Chi-square=0.952; P-value=0.621				

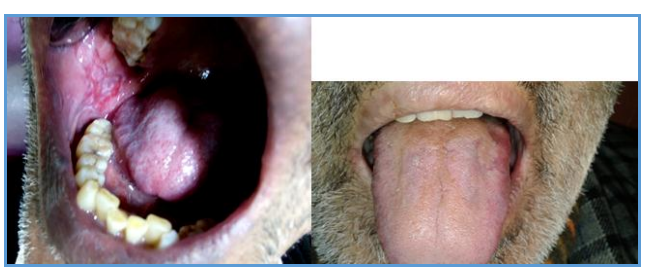
Table 3. Showing Association of Oral Lichen Planus with Gender

Vitamin D Level	Cases [n=20]		Controls [n=20]	
	No.	% Age	No.	% Age
Normal	12	60	18	90
Decreased	8	40	2	10
Total	20	100	20	100
Chi-square=4.80; P-value=0.0285*				

Table 4. Comparison Based on Vitamin D Level among Cases and Controls

*Statistically Significant Difference (P-value<0.05)

Different Clinical Presentations of Oral Lichen Planus Involving Different Sites of Oral Cavity



DISCUSSION

In the present study, it was revealed that the serum vitamin D levels of patients diagnosed with Oral lichen planus, especially the erosive lichen planus was lower than the control group with a few exceptions.

A number of studies in the recent past have shown that Vitamin D has an immune regulatory role.

Vitamin D and its Influence on the Innate Immune System

Certain recent studies have shown how calcitriol enhances the antimicrobial effects of macrophages and monocytes, which are important effector cells, fighting against pathogens such as Mycobacterium tuberculosis. Besides enhancing chemotaxis and phagocytic capabilities of innate immune cells,[11] the complex of calcitriol, VDR, and retinoid X receptor directly activates the transcription of antimicrobial peptides such as defensin β2 (DEFB) and cathelicidin antimicrobial peptide (hCAP18).[12-14] Early evidence that is suggestive of vitamin D acts as an important stimulant for innate immunity came from reports about treatment of tuberculosis with cod liver oil.[15]

Vitamin D and its Influence on the Adaptive Immune System

A number of studies investigating the effects of vitamin D on human adaptive immune cells have demonstrated an expression of the nuclear VDR as well as vitamin D-activating enzymes in both T- and B cells.[16]It has been observed that VDR expression by these cells is very low in resting conditions but upon activation and proliferation, T- and B cells upregulate VDR expression significantly, allowing regulation of up to 500 vitamin D responsive genes which influence differentiation and proliferation of these cells.[17-19]

Antiproliferative effects of calcitriol in B cells such as proliferation, initiation of apoptosis, decreased immunoglobulin production and inhibition of differentiation, were earlier considered to be exclusively indirectly mediated by T helper (Th) cells.[17]

It has been confirmed by certain recent studies regarding the additional direct effects of calcitriol on B cell homoeostasis, including inhibition of memory- and plasma-cell generation, as well as promotion of apoptosis of immunoglobulin-producing B cells.[20] This control on B cell activation and proliferation may be clinically important in autoimmune diseases as autoreactive antibodies produced by B-cells play a major role in the pathophysiology of autoimmunity. The other major type of adaptive immune cells, T cells, is also thought to be an important target for the immunomodulatory effects of different forms of vitamin D. Four probable mechanisms have been proposed[21] by which vitamin D may influence T cell function as mentioned in one of the reviews are as follows-

1. Direct, endocrine effects on T cells mediated via systemic calcitriol.
2. Direct, intracrine conversion of 25(OH) D to calcitriol by T cells.
3. Indirect effects on antigen presentation to T cells mediated via localised APC affected by calcitriol.
4. Direct, paracrine effects of calcitriol on T cells following conversion of 25(OH) D to calcitriol by monocytes or dendritic cells.

Vitamin D and Autoimmune Diseases

Loss of immune homeostasis in autoimmune diseases results in corrupted self-antigen recognition followed by the destruction of body tissue by autoreactive immune cells. A combination triad of genetic predisposition, epidemiological risk factors and environmental factors contributes to the development of autoimmune diseases. An important factor may be the availability of sufficient vitamin D levels as various epidemiological studies highlight the associations between vitamin D deficiency and a higher incidence of autoimmune diseases, such as T1D, MS, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and inflammatory bowel disease (IBD).

CONCLUSION

In the past few decades, research on vitamin D has shown that there are important interactions between vitamin D and cells from the innate as well as from the adaptive immune system. From the data available it can be seen that a variety of tissue cells, including immune cells, express vitamin D metabolising enzymes, are providing a biologically plausible mechanism for local, auto- and paracrine conversion of the native circulating forms, to the active form calcitriol. This emphasises the importance of the process for normal immune function and therefore impaired or insufficient vitamin D levels may lead to dysregulation of immune responses. As per the conclusion drawn in one of the recent

systematic reviews,[22] it was seen that several studies performed over the last 40 years support the role of vitamin D in the prevention of autoimmune diseases but there is still a scarcity of randomised controlled clinical trials in this field. In the future, more and larger clinical trials are needed to determine how vitamin D supplementation affects the pathophysiology of different diseases in vivo and how it may contribute to better efficacy of conventional therapies by immunomodulation. However, keeping in view the emerging trends, current evidence suggests that vitamin D may have a promising role to play and as such it is needed that a study with a larger sample size may be conducted in order to establish the role of vitamin D in the aetiopathogenesis of Oral Lichen planus.

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